

Amendments to the Claims:

This listing of claims will replace all prior versions and listings of claims in the application.

Listing of Claims:

1-153. Cancelled

154. (Currently Amended) The method according to claim ~~[[211]]~~212, wherein said labeling means ~~comprises labeled antigen~~ comprise directly labeled first and second antigens.

155. (Currently Amended) The method according to claim ~~[[211]]~~212, wherein said labeling means ~~comprises a~~ comprise first and second non-immobilized labeled antibody ~~antibodies~~, wherein said ~~non-immobilized labeled antibody binds with~~ said antigen at a which respectively bind said first and second antigens at binding sites distinct from ~~[[a]] the respective binding sites of said first and second antigens~~ for either (i) said autoantibody or the autoantibodies being screened, for or ~~[[ii]] said immobilized antibody or antibodies, whereby in step (d), antigen is allowed to be bound both to said immobilized antibodies and to said non-immobilized antibody.~~

156. (Currently Amended) The method according to claim ~~[[211]]~~212, further comprising providing a control which provides a positive signal in the presence or absence of the autoantibody or autoantibodies being screened.

157. (Currently Amended) The method according to claim 156, wherein the positive control comprises at least one control antibody to at least said first or second the antigen, said control antibody being attached to the substrate, wherein said control

antibody binds to a site on ~~the~~ said first or second antigen distinct from a binding site thereof for the autoantibody ~~or autoantibodies~~ being screened.

158. (Currently Amended) The method according to claim ~~[[211]]~~212, wherein said first and second antigens are ~~[[is a]]~~ distinct thyroid proteins.
159. (Currently Amended) The method according to claim ~~[[211]]~~212, wherein either said first or second antigen is thyroid stimulating hormone receptor.
160. (Currently Amended) The method according to claim ~~[[211]]~~212, wherein said first or second antigen is selected from the group consisting of thyroid peroxidase and thyroglobulin.
161. (Currently Amended) The method according to claim ~~[[211]]~~212, further comprising screening for the presence of at least one of thyroid stimulating hormone, thyroxine, tri-iodothyronine and thyroglobulin in said sample of body fluid.
162. (Currently Amended) The method according to claim ~~[[211]]~~212, wherein said monitoring comprises observing a colorimetric change dependent on said binding of said first and second ~~autoantibody or~~ autoantibodies with said first and second antigens respectively.
163. (Currently Amended) The method according to claim ~~[[211]]~~212, wherein said labeling means is colloidal gold.
164. (Currently Amended) The method according to claim ~~[[211]]~~212, wherein said substrate comprises a membrane of nitrocellulose, cellulose acetate or a polyamide.

165. (Currently Amended) The method according to claim ~~[[211]]~~212, wherein said substrate comprises an application zone provided upstream of said immobilized antibodies on said substrate, and wherein said mixture is allowed to flow from said application zone along said substrate to said immobilized antibodies.
166. (Currently Amended) The method according to claim 165, wherein said application zone contains said source of first and second said antigens, and said mixture is obtained by contacting said sample of body fluid with said first and second antigens in said application zone.
167. (Currently Amended) The method according to claim 166, wherein said substrate further comprises at least first and second ~~one~~ non-immobilized antibody~~[[y]]ies~~ to said first and second antigens, wherein said non-immobilized antibody~~[[y]]ies~~ ~~[[is]]~~ are provided downstream of said antigen source in said application zone.
168. (Currently Amended) A method of detecting in a sample of body fluid ~~[[for]]~~ the presence of at least one of first and second autoantibodies to at least one antigen, which method comprises:
- (a) providing a first antibody to said antigen, wherein said first antibody is immobilized at a discrete detection position on a substrate and binds a first binding site of said antigen;
 - (b) providing a second antibody to said antigen, wherein said second antibody is
 - (i)—labeled to allow detection of autoantibodies when present in said sample,
 - (ii)—binds a second binding site of said antigen and
 - (iii)—is non-immobilized so that said second antibody flows along said substrate according to step (e);
 - (c) providing a source of said at least one antigen, said antigen comprising a first binding site to which either the first autoantibody or the immobilized antibody binds and a second binding site to which either the second autoantibody or the non-immobilized antibody binds;

- (d) contacting said antigen of step (c) with said sample of body fluid and simultaneously or successively said non-immobilized antibody, so as to obtain a mixture wherein said antigen binds with said first and / or second autoantibodies present in said sample of body fluid, and / or said non-immobilized antibody;
- (e) allowing said mixture obtained in step (d) to flow along said substrate of step (a) to said immobilized antibody; and
- (f) monitoring binding of said antigen with either said first and / or second autoantibodies, or said immobilized or non-immobilized antibodies, by detection of the absence or presence of said labeled non-immobilized antibody at said discrete detection position, so as to provide an indication of the presence of said autoantibodies in said sample of body fluid;
- ~~(g)~~ wherein said first and / or second autoantibodies when present in said sample respectively bind with said first and second binding sites of said antigen in step (d) so that respective binding of said immobilized and / or non-immobilized antibodies with said first and second binding sites of said antigen is completely or partially inhibited; and
- wherein (i) in the absence of said first and second autoantibodies said labeled non-immobilized antibody is detectable at said discrete detection position on said substrate, or (ii) in the presence of said first and / or second autoantibodies said labeled non-immobilized antibody is not detectable at said discrete detection position on said substrate, or is detectable at a reduced level compared to (i).

169. (Canceled)

170. (Previously Presented) The method according to claim 168, further comprising providing a control which provides a positive signal in the presence or absence of the autoantibody or autoantibodies being screened.

171. (Previously Presented) The method according to claim 170, wherein said positive control comprises attaching to the substrate at least one control agent that binds to the at least one non-immobilized antibody.

172. (Previously Presented) The method according to claim 168, wherein said antigen is a thyroid protein.
173. (Previously Presented) The method according to claim 168, wherein said antigen is thyroid stimulating hormone receptor.
174. (Previously Presented) The method according to claim 168, wherein said antigen is selected from the group consisting of thyroid peroxidase and thyroglobulin.
175. (Previously Presented) The method according to claim 168, further comprising screening for the presence of at least one of thyroid stimulating hormone, thyroxine, tri-iodothyronine and thyroglobulin in said sample of body fluid.
176. (Previously Presented) The method according to claim 168, wherein said monitoring comprises observing a colorimetric change dependent on said binding of said autoantibody or autoantibodies with said antigen.
177. (Previously Presented) The method according to claim 168, wherein said labeling means is colloidal gold.
178. (Previously Presented) The method according to claim 168, wherein said substrate comprises a membrane of nitrocellulose, cellulose acetate or a polyamide.
179. (Previously Presented) The method according to claim 168, wherein said substrate comprises an application zone provided upstream of said immobilized antibody on said substrate, and wherein said mixture is allowed to flow from said application zone along said substrate to said immobilized antibody.

180. (Previously Presented) The method according to claim 179, wherein said application zone contains said source of said antigen, and said mixture is obtained by contacting said sample of body fluid with said antigen in said application zone.
181. (Previously Presented) The method according to claim 180, wherein said substrate further comprises the non-immobilized second antibody to said antigen, wherein said non-immobilized second antibody is provided downstream of said antigen source in said application zone.
- 182-211. (Canceled)
212. (Currently Amended) A method of screening a sample of body fluid for distinct populations of at least first and second autoantibodies which respectively bind at least first and second distinct antigens, which method comprises:
- (a) providing at least first and second antibodies to said at least first and second distinct antigens, wherein said first and second antibodies are immobilized at first and second discrete detection positions on a substrate;
 - (b) providing one or more sources of said at least first and second distinct antigens, wherein said first antigen comprises a binding site to which either said first autoantibody or said first immobilized antibody binds, and said second antigen comprises a binding site to which either said second autoantibody or said second immobilized antibody binds;
 - (c) contacting said at least first and second antigens of step (b) with said sample of body fluid, so as to obtain a mixture wherein said first and second antigens respectively bind with said first and / or second autoantibodies when present in said sample of body fluid;
 - (d) allowing said mixture obtained in step (c) to flow along said substrate of step (a) to said first and second antibodies immobilized at said first and second discrete detection positions on said substrate;

- (e) providing labeling means directly or indirectly to said first and second antigens respectively so as to enable the presence of said autoantibodies in said sample of body fluid to be detected; and
- (f) monitoring binding of said first and second antigens with either said first and / or second autoantibodies, or said immobilized antibodies, by detection of the absence or presence of said directly or indirectly labeled first and second antigens at said first and second discrete detection positions on said substrate, so as to provide an indication of the presence of said autoantibodies in said sample of body fluid[[;]], wherein said first and second autoantibodies when present in said sample being screened bind with said first and second antigens when a mixture is obtained in step (c), whereby subsequent respective binding of said first and / or second immobilized antibodies with said first and second antigens in step (d) is completely or partially inhibited; ~~substantially inhibited and further characterised in that said first and second immobilized antibodies are provided at discrete first and second positions on said substrate, so that monitoring of respective binding of both said first and second immobilized antibodies with said first and second antigens at said discrete first and second positions thereby enables detection and identification of said distinct populations of first and / or second autoantibodies when present in said sample of body fluid.~~

wherein

- (i) in the absence of said first autoantibody said directly or indirectly labeled first antigen is detectable at said first discrete detection position on said substrate; or
- (ii) in the presence of said first autoantibody said directly or indirectly labeled first antigen is not detectable at said first discrete detection position on said substrate, or is detectable at said first discrete detection position at a reduced level compared to (i); and

wherein

(iii) in the absence of said second autoantibody said directly or indirectly labeled second antigen is detectable at said second discrete detection position on said substrate; or

(iv) in the presence of said second autoantibody said directly or indirectly labeled second antigen is not detectable at said second discrete detection position on said substrate, or is detectable at said second discrete detection position at a reduced level compared to (iii).

213-216. (Canceled).